

REMARKS

I. CLAIM AMENDMENTS

Claim 1 was amended to recite "tiemonium iodide." Applicant submits that the amendment is fully supported by the specification as filed. For example, at page 8 of the application as filed, it recites, in part: " 'non-dye' compounds, including peonidin, oxythiamine, tiemonium iodide, elliptinium acetate and furazolium chloride."

New Claim 21 is supported is fully supported by the specification as filed, for example at page 6, which recites, "The cancerous cells are then detectable by any suitable method..."

Accordingly, claims 1 and 21 are pending in the present application.

II. CLAIM REJECTIONS - 35 U.S.C. § 103(a)

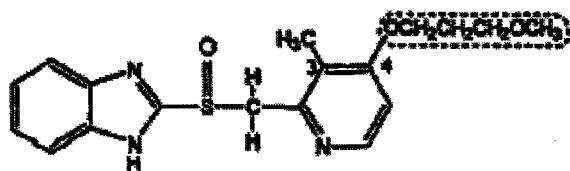
In the Office Action dated October 18, 2007, claim 1 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Pomerantz Edwin WO 9726018 ("Pomerantz") in view of Oseroff et al., Intramitochondrial Dyes Allow Selective *in vitro* Photolysis of Carcinoma Cells, PNAS, December 15, 1986, vol. 83, no. 24, 9729-9733 ("Oseroff"). Specifically, the Examiner recites in part on pages 3 to 4:

Pomerantz teaches in vivo detection (corresponds to step b of claim 1) of oral premalignant lesions and oral carcinomas, including the steps of sequentially rinsing (corresponds to step a of claim 1) the oral cavity with a dye stain composition which is selectively retained by cancerous and precancerous tissues...Pomerantz also disclosed that this type of staining is dependent on the dye gaining access to internal subcellular structures such as the nucleus. Such access is readily obtained only by "fixing" a tissue sample of formaldehyde or other reagent that disrupts the cellular membrane without destroying general cellular structure (page 2, line 26 bridging to page 3, line 4). Note that it is expected that the mitochondria as a subcellular structure would at least partially absorb the dye. Pomerantz did not explicitly teach that the mitochondria is the subcellular structure that will be marked by the dye. Further Pomerantz did not disclose the specific agents in claim 1 as amended.

Oseroff teaches that carcinoma cell mitochondria preferentially accumulate and retain cationic dyes to a much greater extent than most normal cells. In addition, Oseroff teaches that rhodamine and cyanine dyes were tested because they can potentially serve as targets for highly selective photochemotherapy. It is noted that alcian blue dye recited by Applicant in amended claim 1 is a cationic dye.

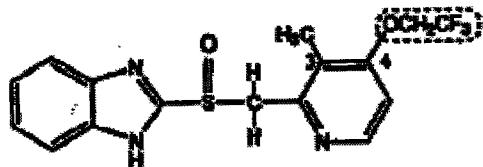
Applicant respectfully disagrees and submits that the present invention as recited in the pending claims is not obvious over Pomerantz in view of Oseroff.

Applicant notes that in *Eisai Co. v. Dr. Reddy Laboratories, Inc.*, the court affirmed the district court's decision that the subject matter of the claims of the patent-in-suit, U.S. Patent No. 5,045,552 ('the '552 Patent) was not obvious. In doing so, the Court illustrated how its approach to chemical obviousness has developed after KSR Int'l Co. v Teleflex Inc ("KSR"). The '552 Patent discloses and claims rabeprazole, the structure of which is depicted below:



### Rabeprazole

The closest prior art cited against the '552 Patent was European Patent No. 0 174 726, claiming lansoprazole, which differs from rabeprazole in having a trifluoroethoxy at the -4 position on the pyridine ring instead of a methoxypropoxy substituent at the -4 position (lansoprazole structure depicted below):



### Lansoprazole

The Court indicated that, when the patent-at-issue claims a chemical compound, the analysis of the third Graham factor (the differences between the claimed invention and the prior art) often turns on the structural similarities and differences between the claimed compound and the prior art compounds. Additionally, the Court further stated that post-KSR, it remains necessary to identify *some reason* that would have led a chemist to

modify a known compound in a particular manner to establish prima facie obviousness of the claimed compound.

In *Eisai*, the Court held that '552 Patent (specifically rabeprazole) was not obvious in view of lansoprazole. The single substitution at the -4 position rendered the claimed invention not obvious.

Here, Claim 1 as amended recites in part, "...contacting said oral epithelium containing cancer cells in the locus of normal cells with one or more agents selected from the group consisting of alcian blue, malachite green, phenosafranin, toluylene blue, brilliant green, peonidin, oxythiamine, tiemonium iodide, elliptinium acetate, and furazolium chloride..." Applicant submits that the structure of each of the claimed compounds differs substantially from the structures of those that are disclosed in the cited art, namely Pomerantz and Oseroff. (See Exhibit A for the structures of each of the claimed compounds and Exhibit B for the structures of the compounds disclosed in Oseroff). The structures disclosed by Pomerantz are depicted in the Abstract.

The difference between the structures of what is claimed and that what is disclosed in the prior art is *much more different* than just a single substitution, i.e., the only difference in *Eisai* between the structure claimed in

the patent-at-issue and the closest prior art is a single substitution at -4. Accordingly, one skilled in the art will appreciate that compounds with different structures are likely to behave differently.

Accordingly, since the Federal Circuit has recently held that a single substitution renders a compound non-obvious, it follows that the present invention, having compounds with significantly different structures than the prior art, and more than single-substitution differences, is non-obvious.

Accordingly, withdrawal of the rejection under 35 U.S.C. § 103(a) is respectfully requested.

### III. CONCLUSION

For the reasons noted above, Applicant respectfully requests that the rejection of claim 1 be reconsidered and withdrawn, and that the pending claims be allowed. It is believed that all claims pending patentably define the subject invention over the prior art of record and are in condition for allowance. Such action is earnestly solicited at the earliest possible date.

### Request for Telephone Conference

If, after considering this Amendment, the Examiner believes that any of the pending claims are not properly allowable, Applicant requests that the Examiner please contact their authorized representative identified below by phone prior to issuing any further Office action for the purpose of hopefully resolving any such issue.

The Commissioner is hereby authorized to charge any

additional fees necessary to Deposit Account 10-0440, or to credit any overpayment to the same.

Respectfully submitted,

Date: August 25, 2008

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